537,607

PCT/EP2003/014678

Translation

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference G 3184 PCT | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
|---|---|---|
| International application No. PCT/EP2003/014678 | International filing date (*day/month/year*) 19 December 2003 (19.12.2003) | Priority date (*day/month/year*) 20 December 2002 (20.12.2002) |
| International Patent Classification (IPC) or national classification and IPC G01N 33/68, 33/573 | | |
| Applicant GSF-FORSCHUNGSZENTRUM FÜR UMWELT UND GESUNDHEIT GMBH | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 28 April 2004 (28.04.2004) | 15 December 2004 (15.12.2004) |
| Name and mailing address of the IPEA/EP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/014678

## I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-22, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 1-15, filed with the letter of 10 November 2004 (10.11.2004)

☒ the drawings:

pages 1/9-9/9, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/014678

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-15 (partially)

because:

☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-15 (partially) .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 03/14678

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-15 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 1-15 | YES |
| | Claims | | NO |
| Industrial applicability (IA) | Claims | 1-15 | YES |
| | Claims | | NO |

2. Citations and explanations

**See the Supplemental Box.**

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1, V.2

The applicant's arguments were taken into account in the establishment of the international preliminary examination report.

**Box III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. In consequence of the very broad claim 13, the amended claims 1-15 relate to an inordinately large number of possible methods, of which only a small proportion are supported by the description (PCT Article 6) and/or can be regarded as having been disclosed in the application (PCT Article 5). In the present case the claims lack the proper support and the application lacks the requisite disclosure to such an extent that it does not appear possible to carry out a meaningful search covering the entire range of protection sought. The search was therefore directed to the parts of the claims that appear to be supported and disclosed in the above sense, namely the parts relating to the examples in which the methods are carried out with antibodies.

It has not been possible to carry out a search covering the entire scope of protection sought, for the following reasons. Firstly, terms which, as also explicitly stated in the application, are not used consistently in the prior art and are therefore not clear, are used. Secondly, these substances are defined functionally in terms of the specific binding to, for example, a fragment of the protein which, as explained below (see item 2.), is not clearly defined

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1, V.2

either (description, page 5, lines 20 to 25: "preferably"). The only clearly defined term is the antibody against GBP-1.

2. In consequence of the use of the unclear term "or fragments of said protein" in claims 1, 4, 7, 9, 10 and 11, the amended claims 1-15 relate to an inordinately large number of possible compounds, of which only a small proportion are supported by the description (PCT Article 6) and/or can be regarded as having been disclosed in the application (PCT Article 5). In the present case the claims lack the proper support and the application lacks the requisite disclosure to such an extent that it does not appear possible to carry out a meaningful search covering the entire range of protection sought. The search was therefore directed to the parts of the claims that appear to be supported and disclosed in the above sense, namely the parts relating to the methods which include the protein itself.

The expression "fragments of said protein" also includes embodiments which do not solve the technical problem (PCT Article 33(3)). It is quite conceivable that fragments neither possess the activity of GBP-1 nor are useful for the detection of an inflammatory disease. This is particularly the case since both functions are disclosed only as preferred embodiments in the description (page 5, lines 20 to 25: "preferably"). Consequently, the term "fragments" is considered to be too broad and the scope of protection is not clearly defined (PCT Articles 5 and 6). The term "guanylate binding protein-1", on the other hand, is sufficiently clear.

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1, V.2

The substantive examination could be carried out only for the above-mentioned searched portion of the application.

**Box V**

**Reasoned statement under PCT Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: American Journal Of Pathology (11-2002), 161(5), 1749-1759
D2: US-A1-2002/115138
D3: Embo Journal, Oxford University Press, Surrey, GB (15-10-2001), 20(20), 5568-5577
D4: Journal Of Biological Chemistry. (microfilms), American Society Of Biological Chemists, Baltimore, MD, US (23-06-1983), 258(12), 7746-7750
D5: Gene (Amsterdam) (1994), 144(2), 295-299.

1. PCT Article 33(2) and (3)

The subject matter of **independent claim 1 is considered to be novel** (PCT Article 33(2)) (see, however, Box III) in relation to the prior art, because no document discloses a method in which guanylate binding protein-1 is detected in the culture supernatant of a tissue sample, a sample of body fluid or a sample of a cell culture supernatant.

D1 discloses Western blotting with a specific monoclonal antibody (1B1; page 1752, column 1, second

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1, V.2

paragraph) for GBP-1 (page 1751, column 1, third paragraph). Since the antibody binds specifically, a specific binding is automatically detected. The binding is detected by means of the Western Blot.

D2 describes the detection and/or quantification of GBP-1, using ELISA for example (page 7, column 2, second paragraph).

D3 discloses the use of a monoclonal antibody against GBP-1 on cells. The binding is detected using the ABC Elite kit and the DAB substrate (page 5576, column 1, first paragraph). In addition, a Western Blot containing a monoclonal antibody is carried out (page 5575, column 2, sixth paragraph).

D4 describes the detection of, for example, GBP-1 (GBP-1 is the 67 kDa protein; see D5, page 295, column 2, second paragraph) using guanylate agaroses, for example the GMP agarose with high affinity for GBPs, in affinity chromatography columns. Protein extracts and a radioactively labelled control are passed through nucleotide affinity columns. The proteins bound in the columns are then eluted and separated and detected in polyacrylamide gels (page 7746, column 2, third paragraph to page 7747, column 1, second paragraph; page 7747, column 2, third paragraph; and additional material to this article (Supplemental Material)).

The same applies to **dependent claims 2-15** (see, however, Box III).

2. The subject matter of independent claim 1 differs from the prior art D1 to D5 in that guanylate binding

**Supplemental Box**
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1, V.2

protein-1 is detected in the culture supernatant of a tissue sample, a sample of body fluid or a sample of a cell culture supernatant.

The technical problem can therefore be considered that of indicating a simplified test for the detection of GBP-1.

The problem is solved as indicated above.

Since no prior art document discloses that GBP-1 can be found in the culture supernatant of a tissue sample, a sample of body fluid or a sample of a cell culture supernatant, a combination of the documents cannot suggest the present solution either. Consequently, the subject matter of **independent claim 1** is considered to be **inventive** (PCT Article 33(3)).

The same applies to **dependent claims 2-15** (see, however, Box III).